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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/847,538	05/03/2001	Brita Schulze	047664-5002-US	4013

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EXAMINER	
SHARAREH, SHAHNAM J	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 01/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/847,538	SCHULZE ET AL.	
	Examiner	Art Unit	
	Shahnam Sharareh	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 October 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *33,37-51 and 53-74* is/are pending in the application.

4a) Of the above claim(s) *37-51 and 70-73* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *33,53-69 and 74* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Amendment filed on October 04, 2004 has been entered. Claims 33, 37-51, 53-74 are pending. Claims 37-51, 70-73 stand withdrawn because they are not directed to elected invention or species. claims 70-73 are not directed to elected species.

2. With respect to the withdrawn claims 37-51, Applicant states that claim 37-51 are now dependent upon claim 58 and that the claim 58 is a necessary process for these products. (see Response at page 9 under the heading Status of the Claims). Applicant then asserts that claim 58 is a linking claim and once found allowable the restriction requirement as to the linked invention must be withdrawn. (see *Id.*).

In response, Examiner states that as the initial matter, claim 58 is not a linking claim. Applicant is referred to MPEP 809.03-04 for proper definitions and examples of linking claims. Claim 58 does not fall into such category because the claim does not contain any limitations that link the claimed process to the claimed product. Claim 58 is merely a process of making or modifying an agent with no links to any of the product claims.

3. Second, claims 37-51 appear to be drafter in the form of "product by process." Examiner states that "product by process" claims are not limited to the manipulations of the recited steps, only the structure implied by the steps. (see MPEP 2113.). "Even though product - by process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product - by - process claim is the same as or obvious from a product of the prior art, the claim is

unpatentable even though the prior product was made by a different process." *In re Thorpe* , 227 USPQ 964, 966 (Fed. Cir. 1985).

Thus, Examiner faces a clear burden of search in order to ascertain the patentability of a product or a process of making such product, because as reasoned in *Thorpe,* the patentability of a product does not depend on its method of production. If the product in the product by process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. Here, as set forth on the record, the claimed product can be prepared by other various other methods known in the art. Therefore, the restriction is proper.

4. Finally, Applicant appears to have confused the principles of rejoinder set forth in the provisions of MPEP 821.04 due to the restriction or record between product and process claims. However, such principles only apply when applicant would have elected claims directed to the product. Subsequently if the product claim is found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04 as a matter of right.

In addition, applicant is informed that until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai*, *In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996).

Here, neither has the product claims been elected for the prosecution on the merits following the restriction requirement, nor does the instant process claims include all limitations of a patentable product. In fact, no product claims have been declared allowable. Therefore, Applicant's arguments for withdrawal of the restriction, even upon allowance of the process claims, are not persuasive.

Claim Rejections - 35 USC § 102

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5. Claim 33 is rejected under 35 U.S.C. 102(b) as being anticipated by Watts et al US Patent 5,840,341 ("Watts").

6. Applicant's arguments with respect to this rejection have been fully considered but are not persuasive. Applicant argues that claim 33 is not directed to methods of identifying zeta potential for compositions targeting an activated vascular site wherein the composition is for vascular endothelial cell uptake. (*see* Arguments at page 10, 3rd para.).

In response Examiner states that the newly added limitations are not viewed to positively limit the method steps of the instant claim, because it merely adds a functional characteristic to the compositions employed. Further, Watts methods inherently meets such limitations. First, Watts teaches determination of zeta potentials at pH 7.4 and 0.1 M ionic strength (*see* col 3, line 65-col 4, line 23). Such zeta potential is within the limitations of the instant claims. Therefore, the method of Watts would produce such

composition comprising chitosan, a cationic component that can target an activated vascular site.

Second, the instant claims are merely limited to a method of measuring a zeta potential for a composition and then identifying an optimal range of the zeta potential. Watts exactly performs such method steps. (see col 4-6). Watts describes preparation of particle compositions crosslinked with a cationic component, measuring its zeta potential and ascertaining that the preferred zeta potential of the particles should be in a range of +1.0 mV to +45 mV at a pH range of about 7.4. (*see* col 5, lines 56-col 6, line 34). Such limitations fall within the scope of the instantly recited zeta potentials. Therefore, the methods of Watts would provide such compositions that would inherently meet all functional limitations of the instant compositions.

7. Applicant has also asserted that Watts is directed to methods of targeting agents to mucosa which is distinct from the route for targeting agents to an activated vasulcar sites. (*see* Arguments at page 11, 2nd para.). In response Examiner first states that the instant claims are not directed to methods of targeting any region, rather the instant claims are methods of identifying an optimal range of zeta potential of a composition wherein the composition is associated with different amounts of cationic components that targets the composition to the activated vascular site. (see claim 33). Therefore, Applicant's arguments are not commensurate with the scope of the rejected claim.

Second, Watts intention of targeting mucosa is not at issue. Rather, whether Watts teach all the elemental steps of the instant claims. Since Watts meets such limitations the compositions prepared by Watts methods would also provide the same

intended purpose as the instantly employed composition. Thus, Examiner views Watts as an art that teaches all elemental steps of the instant claims.

Claim Rejections - 35 USC § 103

8. Claims 53-55, 58-63, 67-69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Watts.

9. Applicant's arguments with respect to this rejection have been fully considered but are not persuasive. Applicant argues that the recited claims are directed to modifying an agent that would target an activated vascular sites and Watts does not teach targeting activated vascular sites. (*see* Arguments at page 12).

In response Examiner state that the teachings of Watts are also directed to methods of making a cationic drug delivery system by measuring zeta potentials for such cationic delivery systems that can comprise antibiotics and antimicrobials such as tetracyclines or antitumor agents. (*see* col 7, lines 13-20). Watts teaches that his drugs including antimicrobial or antitumor agents are associated with cationic particles such as chitosan. (*see* col 7, lines 13-20; col 12, lines 65-67 and the examples).

As argued above, the process described by Watts meets all the limitations of the instant claims. Therefore, the composition obtained in Watts inherently is capable of performing the same function as those instantly employed. Further, antibiotics and antitumor agents target activated vascular sites within the meaning of the instant claims and are up taken at vascular endothelial cell, because they mechanism of actions rests on treating activated vascular site. (*see* for example the instant claim 69 recites such antibiotics and tetracyclines to fall within the scope of composition). Therefore, as

suggested in Watts, modifying Watts compositions to contain an antibiotic or antitumor would have rendered the limitation of the instant claims obvious.

10. In addition, the instant recitation "activated vascular sites" encompass all such areas that an antibiotic or an antitumor agent target, because according to the definition at para 0077 of the instant specification, "activated vascular sites" include areas with "angiogenic endothelial cells." Compositions of Watts containing antibiotics and antitumors target inflamed vasculature. Inflammation at local level follow the process of neovascularization or angiogenesis which inherently leads to the proliferation of endothelial cells at local level.[1] Thus, once the drug delivery of Watts comprise an antibiotic or an antitumor agent, they would have targeted activated vascular sites.

11. As argued above, Watts methods would also target the activated sites encompassed by the instant claims. Watts specifically states that the intended purpose is to improve uptake of therapeutic agents at a site of interest. (col 1, lines 10-15). Accordingly, merely one of ordinary skill in the art would have been motivated to use an antitumor agent or antimicrobial agent to improve delivery to activate vascular sites. Such modifications would render the limitations of the instant process steps obvious.

12. Claims 64-66, 74 are rejected under 35 U.S.C. 103(a) as being unpatentable over Watts as applied to claims 53-55, 58-63, 67-69 and further in view of WO 97/47323 ("WO '323").

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[1] Applicant is noted that extra reference or evidence can be used to show an inherent characteristic of the thing taught by the primary reference. See MPEP § 2124. and Continental Can Co. USA v. Monsanto Co.,20 USPQ2d 1746, 1749 (Fed. Cir. 1991). Accordingly, applicant's attention is drawn to Leibovich et al US Patent 4,808,402 which is used to show that bacterial infections and tumor cells trigger a neovascularization (angiogenesis) process that would lead to mobilization and proliferation of local endothelial cells. (see col 1, lines 1-20, col 6, line 60-col 7, line 61).

The teachings of Watts are described above. Watts fails to describe the use of iron particles.

WO '323 describes that iron and chitosan are compatible for oral delivery. WO '323 teaches the use of iron salt particles in combination with chitosan as microparticles for oral delivery. (see abstract; page 9). WO '323 teaches that iron improves drug entrapment in chitosan powders. (see page 4 line 1). Accordingly, WO '323 provides for improving the delivery of such drugs that are inactived following oral delivery (see page 7, lines 15-36).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time of invention to further add iron to the chitosan of Watts to improve delivery of therapeutic drugs into activated site of interest, because one of ordinary skill in the art would have had a reasonable expectation of success in improving the entrapment of antitumor agents and thus enhance the delivery of such agents that are not active following oral delivery.

Conclusion

No claims are allowed. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action, because they modified the scope of the presented claims. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shahnam Sharareh whose telephone number is 571-272-0630. The examiner can normally be reached on 8:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, PhD can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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